Results: A total of 129 women were included: 85 DMD and 44 BMD carriers. Their mean age was 37 ± 10 years. Mean LV end diastolic diameter (LVED) was 50 ± 5 mm, mean shortening fraction (SF) was 37 ± 7%, and mean E-point septal separation (EPSS) was 5 ± 2 mm. None had more than mild mitral, aortic or tricuspid regurgitation. Fourteen DMD and 4 BMD carriers had LV abnormalities. LV dilatation (LVED > 57 mm) was observed in 8 DMD, reduced SF (< 27%) in 1 BMD and 3 DMD, increased EPSS (> 8 mm) in 1 BMD and 6 DMD, and 4 DMD had regional wall motion abnormalities. Diastolic dysfunction (E/A ratio < 1) was noted in 2 BMD and 2 DMD. Six DMD carriers were considered to have dilated cardiomyopathy.

Conclusion: LV dysfunction is more frequently seen in DMD as compared to BMD carriers. Although most carriers appear to have normal LV function, manifest cardiomyopathy is seen in 7% of DMD carriers.

906-46 Lymphocytic Myocarditis in Childhood: Incidence and Outcome Following Dual Therapy Immunosuppression

Sabine Kleinert, Patricia Kelly, James Wilkinson, Chung-Wo Chow, Robert Weintraub. *Royal Children's Hospital, Melbourne, Australia*

The true incidence of myocarditis in children with acute dilated cardiomyopathy (DCM) is unkown and reported outcome with supportive therapy alone is variable. Although animal models suggest that immune mechanisms play an important role in the pathogenesis of myocarditis, the efficacy of immunosuppression in humans has not been established.

Early endomyocardial biopsy was performed 26 consecutive children with acute DCM. Group I patients (n = 8; 31%) with "definite" myocarditis (lymphocytic infiltrate + myocardial necrosis) were treated with cyclosporine and prednisolone, with follow-up biopsies prior to withdrawal of therapy. Group II patients (n = 3; 11%) with "borderline" myocarditis (lymphocytic infiltrate alone) and Group III (remaining patients; n = 15; 58%) received conventional medical therapy. Echocardiographic Z scores were derived from 300 age-matched control subjects. There were no non-invasive features that distinguished Group I patients from the other groups.

	Group I	Group III	P value
Early LVEDd Z score	5.0 ± 0.6	4.1 ± 0.5	NS
Early FS Z score	−5.2 ± 0.3	−5.9 ± 0.3	NS
Late LVEDd Z score	0.8 ± 0.3*	3.0 ± 0.8	< 0.05
Late FS Z score	−0.9 ± 0.4*	−2.6 ± 0.7	0.06
Echo recovery	8/8	5/15	< 0.05
Death	0/8	4/15	NS

*P < 0.01 by comparison with early Z score

Two Group I patients had late echocardiographic and biopsy worsening which responded to reinstitution of immunosuppression.

Lymphocytic myocarditis is frequent in children with acute DCM. Dual therapy immunosuppression is associated with a favourable outcome. These preliminary data point to the need for a specific controlled trial of dual therapy immunosuppression in paediatric patients.

906-47 Altered Myocardial Phenotype Following Mechanical Support in Humans With Advanced Cardiomyopathy

Gregory Altemose, Vadim Gritsus, Bruce Goldman, Valluvan Jeevanandam, Kenneth Margulies. *Temple University School of Medicine, Philadelphia, PA*

Left ventricular assist devices (LVAD) provide lifesaving circulatory support to patients awaiting orthotopic heart transplantation. To date, the extent to which sustained mechanical unloading alters the phenotype of pathologic myocardial hypertrophy in dilated cardiomyopathy is unknown. Therefore, we examined LV size, myocyte morphometry and atrial natriuretic peptide (ANP) immunoreactivity in eight patients with advanced dilated cardiomyopathy before and after LVAD support. The mean duration of CHF was 18 ± 5 months, and LVAD support averaged 42 ± 4 days prior to heart transplantation.

	Pre-LVAD	Post-LVAD
Mean PA pressure (mmHg)	41 ± 2	23 ± 3*
PA wedge pressure (mmHg)	29 ± 3	17 ± 3*
Cardiac Index (l/min/m^2)	1.9 ± 0.2	2.8 ± 0.2*
LV short axis diameter (cm)	7.8 ± 0.9	5.5 ± 0.5*
LV Mass (grams)	339 ± 60	205 ± 27*
Myocyte diameter (μm)	28.1± 0.9	21.7± 0.6*

All values mean ± SEM, *p < 0.05 vs. Pre-LVAD

As shown above, hemodynamic support and unloading with the LVAD reduced echocardiographically determined LV dilation and LV mass. Minimum myocyte diameter at the level of the nucleus also decreased following LVAD support. Overall left ventricular ANP immunopositivity decreased from 48% at LVAD placement to 12% at transplantation (p < 0.05), and there was a close correlation (r = 0.82, p < 0.001) between left ventricular mass and ANP immunopositivity before and after LVAD support. These studies demonstrate remarkable LV plasticity even in the presence of advanced cardiomyopathy. Reductions in ventricular ANP immunostaining also suggest that LVAD support induces a unique change in the phenotype of pathologic cardiac hypertrophy.

906-48 Idiopathic Familial Dilated Cardiomyopathy: Identifying Early Disease in Asymptomatic Relatives

M. Kamran Baig, Jonathan H. Goldman, Philip J. Keeling, Aman S. Coonar, Mitsutoshi Yamada, Alida L.P. Caforio, William J. McKenna. *St Georges Hospital, London, UK*

Background — Familial disease is present in > 25% of patients with dilated cardiomyopathy (DCM). The ability to identify asymptomatic relatives with early disease is a major goal in understanding pathogenesis and improving management.

Method — We assessed 321 asymptomatic relatives (mean age 35 ± 15, 193 male) of 70 DCM patients (WHO criteria).

Results — 59 (20%) had LV enlargement (LVE = > 112% predicted LVEDd), 21(7%) had depressed fractional shortening (dfs = FS < 25%) and the remainder had normal dimensions and contractility (NOR). Diastolic dysfunction (AbN E/A ratio) was present in 40 (68%) LVE relatives and 60(41%) NOR. LVE's had lower FS (33 ± 5% vs 35 ± 6%, p < 0.05), and longer total QRS (98 ± 12 ms vs 94 ± 10 ms, p = 0.05), than those with normal echos. A greater proportion of LVE had abnormal VO_2 Max (< 80% predicted) compared to NOR (6.10% vs 7.4%; p < 0.05). Dfs's had larger LVDd% predicted (112 ± 13 vs 102 ± 7, p < 0.001), and lower RMS voltage (34 ± 18 mv vs 58 ± 40 mv, p = 0.05) than NOR. The mean E/A ratio of relatives (n = 100) was lower than predicted E/A ratio, (1.55 ± 0.83 vs 1.75 ± 0.44, p = 0.03) and LVE had lower E/A ratio than NOR (1.29 ± 0.72 vs 1.60 ± 0.71, p = 0.04). Over 27.5 ± 14.3 months follow-up, 9 relatives developed DCM and one (with mild palpitations) died suddenly.

Conclusions —Asymptomatic relatives commonly have echocardiographic abnormalities; the metabolic and SA-ECG abnormalities also observed suggest these two echo abnormalities may represent early DCM.

906-49 Chronic Adenosine Receptor Blockade Prevents Attenuation of Adrenergic Responsiveness in Left Ventricular Hypertrophy

Eugene S. Chung, Theo E. Meyer, James G. Dobson Jr, Richard A. Fenton, Gerard P. Aurigemma, William H. Gaasch. *University Massachusetts Medical Center, Worcester, MA*

Left ventricular hypertrophy (LVH) is associated with reduced adrenergic responsiveness (AR). Acutely, adenosine (ADO) levels increase in response to increased myocardial work and exhibit an antiadrenergic action. To determine whether chronic blockade of the ADO receptor or ADO uptake would alter AR in LVH, rats with LVH, induced by suprarenal aortic banding (B), and sham operated rats (S) were each subdivided into 3 treatment groups, with the last dose given 24 hours before sacrifice: theophylline (ADO receptor blocker; 20 mg/kg ip bid, groups BT, ST), dipyridamole, (ADO uptake blocker; 5 mg/kg ip bid, groups BD, SD), or 0.9% NaCl (2 ml/kg ip bid, groups BN, SN). At 9 weeks, hearts were perfused with physiological saline solution at a pressure predetermined by the carotid blood pressure. AR to isoproterenol was assessed at 4 doses. Data are shown as mean ± SEM; MBP = Mean BP (mmHg); LVwt = dry LV weight (mg/g body weight); ΔdP/dt = maximal change in +dP/dt (mmHg/s); EC_{50} = log M concentration at 50% of maximal response;

	BT(n21)	BD(n19)	BN(n16)	ST(n16)	SD(n16)	(SN(n17)
MBP	134 ± 5†	125 ± 9†	137 ± 6†	94 ± 5	92 ± 4	106 ± 4
LVwt	0.57 ± 0.02†	0.58 ± 0.02†	0.61 ± 0.02†	0.42 ± 0.01	0.41 ± 0.01	0.41 ± 0.01
ΔdP/dt	3587 ± 161	2832 ± 286†	2999 ± 212†	4461 ± 270	4020 ± 369	4149 ± 258
EC_{50}	−8.14 ± 0.02	−8.05 ± 0.07*	−8.14 ± 0.03	−8.21 ± 0.03	−8.23 ± 0.02	−8.23 ± 0.02

†p < 0.0001; * p < 0.05 vs. respective sham controls.

Conclusions: Data confirm reduced AR in LVH. Chronic blockade of ADO uptake reduces the AR, while chronic receptor blockade prevents attenuation of AR in LVH.

MONDAY POSTER